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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/781,592	02/12/2001	Beverly M. Emerson	1211.003US1	1304

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EXAMINER	
MARVICH, MARIA	

ART UNIT	PAPER NUMBER
1636	

DATE MAILED: 03/16/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/781,592	EMERSON, BEVERLY M.	
	Examiner	Art Unit	
	Maria B. Marvich, PhD	1636	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *02 February 2005*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *38-43,45-51,53-61,63-66,68,69,71-77,79-85 and 87-99* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *38-43,45-51,53-61,63-66,68,69,71-77,79-85 and 87-99* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

This office action is in response to a response to an amendment filed 2/2/05 and request for continued examination filed 11/8/04. A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 11/8/04 has been entered. Claims 1-37, 44, 52, 62, 67, 70, 78 and 86 have been cancelled. Claims 89-99 have been added. Claims 38-43, 45-51, 53-61, 63-66, 68, 69, 71-77, 79-85 and 87-99 are pending in the application.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 38-43, 45-51, 53-61, 63-66, 68, 69, 71-77, 79-85 and 87-99 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 38 and 45 are vague and indefinite in that the metes and bounds of "a specific DNA" are unclear. The claim recites use of a "specific DNA" but the significance of the DNA is unclear given that the method steps do not utilize DNA. Furthermore, if the DNA is to be "a specific DNA", applicants have provided no guidance on the requirements or nature of the DNA such that its specificity is known. **This is a new rejection.**

Claims 38, 45, 63 and 71 are vague and indefinite in that the metes and bounds of "associate with" and "interaction" are unclear. The degree of association or interaction is unclear. Must the domain and subunit be in direct association (i.e. physical contact) or is an indirect association or interaction sufficient. **This is a new rejection.**

Claims 38 and 45 are vague and indefinite in that the metes and bounds of the method are unclear. The preamble states methods of identifying compounds that modulates chromatin remodeling. The method steps are designed to indicate a compound that modulates the interaction between subunits of SWI/SNF or ISWI and domains of proteins. However, a method step for the identification of a compound that necessarily modulates chromatin remodeling is missing. Chromatin remodeling is a complex process requiring the interaction of multiple components. A demonstration of modulators of the interaction between two compounds is not necessarily an indication of an ability to remodel chromatin. **This is a new rejection.**

Claim 89 recites the limitation "The new method" in claim 45. There is insufficient antecedent basis for this limitation in the claim. **This is a new rejection necessitated by applicants' amendment.**

Claim Rejections - 35 USC § 112, first paragraph

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 45, 54-61, 71 and 80-99 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter,

which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. **This is a new rejection.**

Applicants claim a method of screening for test compounds that modulate chromatin remodeling. As a necessary element of the invention, applicants recite use of ISWI subunits that associate with domains of nuclear regulatory proteins. Therefore, applicants claim a genus of ISWI subunits in association with domains of nuclear regulatory proteins.

The written description requirement for genus claims may be satisfied through sufficient description of a representative number of species by actual reduction to practice, reduction to drawings, or by disclosure of relevant identifying characteristics, i.e. structure or other physical and/or chemical properties, by functional characteristics coupled with known or disclosed correlations between function and structure, or by a combination of such characteristics sufficient to show that the applicant was in possession of the claimed genus.

In the instant case, applicants do not disclose any subunits of ISWI. The specification only teaches that ISWI complexes are composed of multiple subunits but the following examples relate only to the subunits of SWI/SNF. The post filing art reveals that several of the subunits became known and these are hACF1, hSNF2H, p17 and p15. However, even then the role in transcriptional modulation or the ability of the domains to interact with nuclear regulatory proteins was not taught (see Peterson, EMBO, 2002). Furthermore, the specification does not disclose a known correlation and function between subunits of a SWI/SNF and subunits from ISWI. The specification does not teach the structure of the ISWI subunits nor provide a description of the structural identifying features for ISWI that are required for interaction with

nuclear regulatory proteins. The specification teaches a variety of subunits of SWI/SNF and teaches that these subunits interact with a variety of transcription factors. Neither applicant nor the prior art provide a correlation between the subunits that interact with nuclear regulatory proteins and those of ISWI. Given the lack of structural-functional relationship between the subunits and their ability to associate with regulatory proteins and the inability to determine which ISWI subunits will interact with any regulatory proteins, it is concluded that the invention must be empirically determined. In an unpredictable art, the disclosure of no species would not represent to the skilled artisan a representative number of species sufficient to show applicants were in possession of claimed genus.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.
>
> (e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

Claims 38-40, 43, 48, 53 and 57-61 are rejected under 35 U.S.C. 102(e) as being anticipated by Wong et al (US 6,465,629; see entire document). **This is a new rejection**.

Wong et al teach a method of screening drugs that modulate the binding of Rb, with BRG1, a chromatin remodeling subunit of SWI/SNF. Rb or retinoblastoma tumor suppressor is

a nuclear regulatory protein that comprises an A and B pocket domain that interacts with chromatin remodeling subunits as well as other transcription factors such as E2F to modulate their activity. The method measures the extent of binding that is enhanced or inhibited by an agent *in vitro* (see e.g. col 27, line 52-col 29, line 3 and col 28,line 55-61). In the method, BRG1 or the nuclear regulatory protein may be tagged with a label (col 28, line 6-32). Small molecules as well as peptides can be identified that modulate the interaction between Rb and BRG1 (see e.g. col 29, line 51-56). As well, Wong teaches that ligands, which have peptide domains, interact with BRG1.

The instant claims recite that the chromatin remodeling subunit is associated with a domain of a nuclear regulatory protein whose interaction is enhanced or repressed by the test compounds. It is unclear if the association and interaction is indirect or not. Therefore, the association of E2F with BRG1-Rb complex includes an association of DNA binding domains, which is a winged helix DNA binding motif that binds to promoter regions.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 63, 64, 66, 69, 74, 84, 85, 87 and 88 are rejected under 35 U.S.C. 103(a) as being unpatentable over Wong et al (US 6,465,629; see entire document) in view of Peterson and

Logie (US 5,972,608; see entire document) further in view of Kadonaga (Cell, 1998, pages 307-313;see entire document). **This is a new rejection.**

Applicants claim a method of screening for compounds that modulate chromatin remodeling of a specific DNA sequence within chromatin by determining chromatin remodeling the presence of a SWI/SNF complex with a nucleic acid regulatory protein.

The teachings of Wong et al are described above and are applied as before except;

Wong et al do not teach that assaying chromatin remodeling identifies the drug.

Peterson and Logie et al teach methods of screening candidate modulators of chromatin remodeling enzymes such as SWI/SNF in which the nucleosome array is incubated with SWI/SNF in the presence and absence of candidate modulators (see e.g. col 3, line 44-62). The assays are said to be simple, rapid easily quantitated and utilizes a substrate that resembles or mimics physiological chromatin (see e.g. col 4, line 23-31). The nucleosome array comprises DNA from 5S repeats (see e.g. example 1). High throughput screening methods are taught (see e.g. col 9, line 39-col 10, line 9).

Kadonaga teaches that a widely used assay that detects changes in histone DNA interaction is a DNAse I hypersensitivity assay (see e.g. page 310, col 2). Furthermore, Kadonaga teaches that this assay has the added benefit of detecting the ability of remodeling factors to facilitate the binding of transcription factors to mononuculeosomes (see e.g. page 311, col 1).

It would have been obvious to one of ordinary skill in the art at the time the invention was made to use the chromatin remodeling assay as Peterson and Logie et al further in view of the DNAse I assay taught by Kadonaga to assay the effects of compounds on the ability of BRG1

and Rb to interact because Wong et al teach that is within the ordinary skill in the art to identify modulators of BRG1 interaction with Rb and Peterson and Lorie teach that it is within the ordinary skill of the art to use chromatin remodeling as an assay for drugs that effect SWI/SNF function and Kadonaga teaches that it is within the ordinary skill in the art to assay chromatin remodeling using DNAse I. One would have been motivated to do so in order to receive the expected benefit of a simple, rapid easily quantitated assay for drugs that effect chromatin remodeling as taught by Peterson and Logie with the ability to detect the ability of remodeling factors to facilitate the binding of transcription factors to mononuculeosomes as taught by Kadonaga. Based upon the teachings of the cited references, the high skill of one of ordinary skill in the art, and absent evidence to the contrary, there would have been a reasonable expectation of success to result in the claimed invention.

Claims 41, 47, 53-57, 65, 73 and 80-83 are rejected under 35 U.S.C. 103(a) as being unpatentable over Wong et al (US 6,465,629; see entire document) in view of Strober et al (MCB, 1996, pages 1576-1583; see entire document). **This is a new rejection.**

Applicants claim a method of screening for compounds that modulate chromatin remodeling of a specific DNA sequence within chromatin by determining chromatin remodeling the presence of BRM with a nucleic acid regulatory protein.

The teachings of Wong et al are described above and are applied as before except;

Wong et al do not teach that that the method uses BRM.

Strober et al teach that BRM interacts with Rb to induce flat, growth arrested SW 13 cells. Following interaction of BRM with RB, glucocorticoid mediated transcriptional activation

is then potentiated (see e.g. page 1577, col 1, paragraph 2). As BRG1 interaction with Rb mediates its effects through E2F, the multiple pathway options appear to present a fine regulation of transcription by utilizing a multiplicity of possible interactions (see e.g. page 1582, col 1, paragraph 3). The instant claims recite that the chromatin remodeling subunit is associated with a domain of a nuclear regulatory protein whose interaction is enhanced or repressed by the test compounds. It is unclear if the association and interaction is indirect or not. Therefore, the association of GR with BRG1-Rb complex includes an association of DNA binding domains, which is a zinc finger motif.

It would have been obvious to one of ordinary skill in the art at the time the invention was made to perform the assay for drugs that alter Rb binding to BRG1 as taught by Wong et al using BRM as taught by Strober et al et al because Wong et al teach that is within the ordinary skill in the art to identify modulators of Rb binding to identify drug therapies for cancer and Peterson and Lorie teach that it is within the ordinary skill of the art to assay BRM, Rb interaction. One would have been motivated to do so in order to receive the expected benefit of identifying modulators of fine regulation of transcription by affecting a multiplicity of possible interactions. Based upon the teachings of the cited references, the high skill of one of ordinary skill in the art, and absent evidence to the contrary, there would have been a reasonable expectation of success to result in the claimed invention.

Conclusion

No claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Maria B. Marvich, PhD whose telephone number is (571)-272-0774. The examiner can normally be reached on M-F (6:30-3:00).

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Remy Yucel, PhD can be reached on (571)-272-0781. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Maria B Marvich, PhD
Examiner
Art Unit 1636

March 12, 2005

GERRY LEFFERS
PRIMARY EXAMINER